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EXAMINER	
MYERS, CARLA J	
ART UNIT	**PAPER NUMBER**
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SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,197	CROSSMAN ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group IV, claims 8-10 and 12-15, kits comprising primers that hybridize to IL-1RN (VNTR) allele 1, and of the particular primer of SEQ ID NO: 7 in the reply filed on October 26, 2006 is acknowledged.

Claim Objections

2. Claims 8-15 are objected to because the claims include subject matter of the non-elected inventions, namely the additional alleles of Il-1A (+4845), IL-1B (-511), IL-1B (+3954), and IL-1RN (+2018). In response to this Office action, the claims should be amended so that they are limited to the elected invention of the IL-1RN (VNTR) allele.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed - i.e., kits for determining susceptibility to restenosis.

Priority

4. The present claims are entitled to priority to application 09/578,534, filed May 24, 2000. The present claims are not entitled to priority to parent applications 09/431,352, 09/320,395 or 08/813,456 because these applications do not appear to provide support for the presently claimed subject matter of kits for determining the existence of susceptibility to developing restenosis in a subject wherein said kit comprises a primer that hybridizes 5' or 3' to a IL-1RN (VNTR) allele 1. Additionally, it is noted that a claim

as a whole is assigned an effective filing date, rather than the subject matter within a claim being assigned individual effective filing dates.

Claim Rejections - 35 USC § 112 Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite over the recitation of "said first primer and said second primer hybridize to a region in the range of between about 50 and 1000 base pairs" because it is not clear as to what is meant by this phrase. This phrase is not clearly defined in the specification and there is no art recognized definition for this phrase. Accordingly, it is unclear, for example, as to whether the primers hybridize to any sequence within a range of 50 to 1000 base pairs such that both primers hybridize to a contiguous region having a length of between 50 to 1000 base pairs, or whether the primers hybridize to a region so as to generate an amplification product of 50 to 1000 base pairs, or whether each primer individually may hybridize to any region that spans 50 to 1000 base pairs.

Claim 13 is indefinite over the recitation of "the detection means is selected from the group consisting of: allele specific hybridization, size analysis..." because the recited list consists of methods, rather than detection means. While it is clear as to what

is intended to be meant by a kit comprising reagents for performing a method, it is unclear as to what is intended to be meant by the kit comprising the stated methods.

Claim Rejections - 35 USC § 112 - Written Description

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **Written Description** rejection.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a

nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the claims are drawn broadly to encompass kits comprising a first primer that hybridizes 5' or 3' to an IL-RN (VNTR) allele 1 or to any allele that is in linkage disequilibrium with this allele. The claims do not define the primers in terms of any particular structural features, such as the coding or noncoding sequence to which the primers hybridize, the location within the coding or noncoding region to which the primers hybridize etc. Further, the claims do not define the allele in linkage disequilibrium with the IL-RN (VNTR) allele in terms of any particular structural features, such as the gene in which it is located, its position within a gene, the identity of the nucleotide, etc.

The specification (Figure 3) teaches the nucleotide sequence of the IL-1RN gene. The specification (page 66-67) further teaches that the IL-1RN (VNTR) allele 2 is associated with a lower restenosis rate in patients with SVD. The specification (page 11) also discloses primers consisting of SEQ ID NO: 7 and 8 and the use of these primers to amplify sequences comprising the IL-RN (VNTR) allele. Accordingly, the specification provides adequate written description for kits for determining an increased likelihood of a human subject with SVD having or being predisposed to restenosis

wherein said kit comprises a primer that hybridizes 5' or 3' to a IL-1RN (VNTR) allele 1, particularly wherein said primer comprises SEQ ID NO: 7.

Regarding alleles in linkage disequilibrium with IL-1RN (VNTR) allele 1, the specification states that IL-1RN (VNTR) allele 1 is in 100% linkage disequilibrium with IL-1RN (+2018) allele 1. The specification (page 9) also teaches a 33221461 haplotype that comprises the following alleles which are to some degree in linkage disequilibrium with one another: allele 3 of the 222/223 marker ofIL-1A; allele 3 of the gz5/gz6 marker ofIL-1A; allele 2 of the -889 marker of IL-1A; allele 2 of the +3954 marker of IL-1B; allele 1 of the -511 marker ofIL-1B; allele 4 of the gaat.p33330 marker; allele 6 of the Y31 marker; and allele 1 of the VNTR marker of IL-1RN (VNTR). Thereby, the specification teaches 1 additional allele, IL-1RN (+2018) which is in 100% linkage disequilibrium with IL-1RN (VNTR) and which thereby is presumably associated with increased risk of restenosis in human subjects having SVD. While the specification teaches 7 additional alleles in the 33221461 haplotype which are to some degree in linkage disequilibrium with one another, the specification has not established that these 7 additional alleles have the property of being correlated with susceptibility to having or developing restenosis.

It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. restriction map, biological activity of an encoded protein product, etc.). In the instant case, no such identifying characteristics have been provided for any alleles in linkage disequilibrium with IL-1RN (VNTR).

However, the claims as written are inclusive of a potentially large genus of alleles in linkage disequilibrium with IL-1RN (VNTR) and thereby a potentially large genus of primers which hybridize 5' or 3' to an undefined allele in linkage disequilibrium with the IL-1RN (VNTR) allele 1. The claims do not define the alleles in linkage disequilibrium with the IL-1RN (VNTR) allele in terms of any specific identifying features, such as the gene in which it is located, its location/position within a gene, or its nucleotide identity. Further, claims 8-10 and 12-15 do not define the primers in terms of any particular structural features, since the primers may hybridize to any sequence (i.e., any gene or noncoding region) that is 5' or 3' of the IL-1RN (VNTR) allele 1 or any allele in linkage disequilibrium with the IL-1RN (VNTR). Yet, the coding and non-coding sequences of genes that are 5' and 3' of the IL-1A gene have not been described in the specification.

While the sequence of the IL-1RN gene was known in the art at the time the invention was made, this disclosure does not allow the skilled artisan to envision all of the contemplated primers which may hybridize 5' or 3' to this gene. Further, while the identity of the IL-1RN (VNTR) allele was known in the art, this information does not allow one to envision specific polymorphisms that are in linkage disequilibrium with the IL-1RN (VNTR) allele and which could thereby be used to develop primers that hybridize 5' or 3' to the undefined polymorphism. The information provided regarding the IL-1RN (VNTR) allele does not constitute an adequate written description of the broadly claimed subject matter, such that one of skill in the art could readily envision the detailed chemical structure of the nucleic acids encompassed by the claims. Adequate written description requires more than a mere statement that such nucleic acids are part

of the invention and reference to a potential method for identification. The particular nucleic acids are required.

Thereby, the disclosure in the specification of two primers (SEQ ID NO: 7 and 8) which hybridize 5' and 3' to the IL-1RN (VNTR) allele is not considered to constitute a representative number of primers that may hybridize to any coding or non-coding sequence 5' or 3' of the IL-1RN (VNTR) allele or any primers that may hybridize 5' or 3' to any allele in linkage disequilibrium with the IL-1RN (VNTR) allele. For these reasons, Applicants have not provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 112 - Enablement

7. Claims 8-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for kits for determining whether a SVD patient has or is predisposed to developing arterial restenosis wherein the kits comprise a primer consisting of SEQ ID NO: 7 or 8 and wherein said primer hybridizes 5' or 3', respectively, to IL-1RN (VNTR) allele 1, does not reasonably provide enablement for kits for detecting susceptibility to restenosis in any human or non-human subject and/or kits comprising primers which hybridize 5' or 3' to IL-RN (VNTR) allele 1 or any allele in linkage disequilibrium with IL-1RN (VNTR). The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

Claims 8-15 are drawn broadly to encompass kits for detecting susceptibility to restenosis in any human or non-human subject and/or kits comprising primers which hybridize 5' or 3' to IL-RN (VNTR) allele 1 or any allele in linkage disequilibrium with IL-1RN (VNTR). Accordingly, the claims encompass:

i) Kits for the diagnosis of restenosis in any subject, including human subjects with SVD, human subjects with MVD and non-human subjects.

ii) Kits comprising primers that hybridize 5' or 3' of any allele in linkage disequilibrium with the IL-1RN (VNTR) allele 1. The claims do not define the any allele in linkage disequilibrium with the IL-1RN (VNTR) allele 1 in terms of any particular structure - e.g., the gene in which the allele is present, the location of the allele, the identity of the polymorphic nucleotide within the allele.

iii) With respect to claims 8-10 and 12-15, kits comprising primers which hybridize to any coding or non-coding sequence that is 5' or 3' upstream of an IL-1RN (VNTR)

allele 1 or an allele in linkage disequilbrium with an IL-1RN (VNTR) allele 1. The claims do not define the primer in terms of its structural properties, such as the sequence of the primer, the gene to which the primer hybridizes, or the location within a gene to which the primer hybridizes.

Nature of the Invention

The claims encompass kits for determining whether a subject has an increased risk of having or developing restenosis. The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

Teachings in the Specification and State of the Art:

The specification (Figure 3) teaches the nucleotide sequence of the IL-1RN gene. The specification (page 66-67) further teaches that the IL-1RN (VNTR) allele 2 is associated with a lower restenosis rate in patients with SVD. The specification (page 11) also discloses primers consisting of SEQ ID NO: 7 and 8 and the use of these primers to amplify sequences comprising the IL-RN (VNTR) allele.

However, the specification also teaches that no significant association was found between the occurrence of IL-1RN(VNTR) allele 2 and restenosis in MVD patients (see page 66 and Table I).

Accordingly, the specification has enabled kits for diagnosing an increased risk of restenosis in human subjects having SVD wherein the kits comprise an oligonucleotide consisting of SEQ ID NO: 7 or 8, wherein said oligonucleotide hybridizes 5' or 3' to the

IL-1RN (VNTR) allele 1. However, the specification is not enabling for kits for diagnosing an increased risk of restenosis in any human or non-human subject wherein the kits comprise an oligonucleotide that hybridizes to any nucleic acid sequence 5' or 3' to a IL-1RN (VNTR) allele 1 or any allele in linkage disequilibrium to the IL-1RN (VNTR) allele 1.

Regarding alleles in linkage disequilibrium with IL-1RN (VNTR) allele 1, the specification states that IL-1RN (VNTR) allele 1 is in 100% linkage disequilibrium with IL-1RN (+2018) allele 1. The specification (page 9) also teaches a 33221461 haplotype that comprises the following alleles which are to some degree in linkage disequilibrium with one another: allele 3 of the 222/223 marker of IL-1A; allele 3 of the gz5/gz6 marker ofIL-1A; allele 2 of the -889 marker of IL-1A; allele 2 of the +3954 marker of IL-1B; allele 1 of the -511 marker of IL-1B; allele 4 of the gaat.p33330 marker; allele 6 of the Y31 marker; and allele 1 of the VNTR marker of IL-1RN (VNTR). Thereby, the specification teaches 1 additional allele, IL-1RN (+2018) which is in 100% linkage disequilibrium with IL-1RN (VNTR) and which thereby is presumably associated with increased risk of restenosis in human subjects having SVD. While the specification teaches 7 additional alleles in the 33221461 haplotype which are to some degree in linkage disequilibrium with one another, the specification has not established that these 7 additional alleles have the property of being correlated with susceptibility to having or developing restenosis.

The Predictability or Unpredictability of the Art and Degree of Experimentation:

The art of establishing an association between a polymorphism and the occurrence of a disease or disorder is highly unpredictable. While some interleukin polymorphisms, particularly polymorphisms associated with increased interleukin production, have been found to be associated with some inflammatory diseases, there is no universal association established between the presence of these polymorphisms and the occurrence of all inflammatory diseases. The unpredictability of extrapolating the results obtained with the IL-1RN (VNTR) allele 1 to other disorders and to other populations is supported by the teachings in the specification. As discussed above, the specification teaches that while the IL-1RN (VNTR) allele 1 is associated with increased risk of having or developing restenosis in subjects having SVD, the IL-1RNA (VNTR) allele 1 is not associated with risk of restenosis in subjects having MVD. Thereby, the results obtained regarding an association between the IL-1RN (VNTR) and restenosis in SVD human subjects cannot be extrapolated to restenosis in any human or non-human subject.

Further, it is highly unpredictable as to whether the results obtained with the IL-1RN (VNTR) allele can be extrapolated to other alleles in linkage disequilibrium with the IL-1RN (VNTR) allele.

The specification (page 66) states that "(t)he Mantel-Haenzel results summarized over the Leicester and Sheffield cohorts showed no significant differences in genotypic distributions at the IL-1A (-889), IL-1B (+3954), and IL-1B (-511) loci between restenosers and non-restenosers (Table II)". Accordingly, alleles which are considered to be in linkage disequilibrium with IL-1RN (VNTR) were found to show **no correlation**

with restenosis. This finding also underlies the unpredictability in the art of cardiovascular disease diagnosis in that it clarifies that there is not a universal association between IL-1 alleles and the occurrence of restenosis and that it is highly unpredictable as which additional alleles, if any, could be used to determine susceptibility to restenosis.

Additional evidence of the unpredictability in the art of establishing a correlation between IL-1 alleles and restenosis is found in the specification which provides teachings which are directly contradictory to the findings set forth on pages 66 and 67 of the specification. In particular, page 88 of the specification states that "**allele 2** of the 4845, -511, +3954 and VNTR markers in the IL-1RN gene will be over-represented in restenosis". Yet, the 33221461 haplotype which includes the IL-1RN (VNTR) allele 1 also includes **allele 1** IL-1B (-511).

The findings presented in U.S. Patent No. 6,210,877, of which some of the present inventors are co-inventors, further establish the unpredictability of using alleles in linkage disequilibrium as a means for diagnosing susceptibility to cardiovascular disease. This reference (column 8) teaches that IL-1RN (VNTR) allele 2 is present in 41% of single vessel coronary artery disease patients and present in only 21% of control patients. However, this reference also teaches that there was no significant correlation between the IL-1A -889 polymorphism or the IL-1B +3954 polymorphism and single vessel coronary artery disease. The -889 and +3954 polymorphisms are part of the 44112332 haplotype containing IL-1RN (VNTR) allele 2 (i.e., the haplotype disclosed in the present specification as being associated with the IL-1RN allele). Since

even polymorphisms within the same haplotype are not correlated with single vessel coronary artery disease, it is unpredictable as to whether the results obtained with IL-1RN (VNTR) alleles can be extrapolated to other alleles that are to some degree in linkage disequilibrium with the IL-1RN (VNTR) allele. Further, Francis (column 10) teaches that while the IL-1B -511 allele 2 is associated with multiple coronary artery disease, other polymorphisms in the interleukin haplotype, including IL-1A -889, IL-1B +3954 and IL-1RN (VNTR) were not correlated with multiple coronary artery disease. These results further establish the unpredictability of using alleles in linkage disequilibrium with IL-1RN (VNTR) allele as diagnostic markers for restenosis. Moreover, the difference in results observed between multiple vessel coronary artery disease and single vessel coronary artery disease is evidence of the fact that the results obtained with one type of cardiovascular disease cannot be extrapolated to other types of cardiovascular disease.

Additionally, the art of identifying polymorphisms that are in linkage disequilibrium with IL-1RN (VNTR) alleles is also highly unpredictable. Knowledge of the sequence of a wildtype gene, such as IL-1B or other interleukin genes does not allow one to immediately envision specific mutations or haplotypes that are in full linkage disequilibrium with the IL-1RN (VNTR) allele and which could be used in place of the IL-1RN (VNTR) allele to diagnose a restenosis.

The specification suggests that the Il-1RN (VNTR) polymorphism is in linkage disequilibrium with the 33221461 haplotype (see page 9).However, no data is presented

in the present specification regarding an association between individual alleles in this haplotype and restenosis.

Regarding claims 8-10 and 12-15, these claims encompass primers which hybridize to any nucleotide sequence that is 5' or 3' of the IL-1RN (VNTR) allele 1 or an allele in linkage disequilibrium with the IL-1RN (VNTR) allele 1. The claims do not define the primers in terms of the gene sequence to which they hybridize. Thereby, the claims encompass primers that hybridize to any degree to any coding or non-coding sequence that is 5' or 3' of the IL-1RN (VNTR) allele 1 or any undefined allele that is in linkage disequilibrium with the IL-1RN (VNTR) allele 1. The specification does not teach the nucleotide sequences of non-IL-1RN genes that are 5' or 3' of the IL-1RN (VNTR) allele 1 or of other genes that are 5' or 3' of the undefined allele in linkage disequilibrium with the IL-1RN (VNTR) allele 1. Thereby, it is highly unpredictable as to what would be the identity of additional primers that could be used to amplify the IL-1RN (VNTR) allele 1 or an allele in linkage disequilbrium with the IL-1RN (VNTR) allele 1.

Amount of Direction or Guidance Provided by the Specification:

The specification teaches only 1 group of subjects, i.e. humans having SVD, in which the IL-1RN (VNTR) allele 1 is associated with restenosis. The specification does not provide any specific guidance as to other specific populations or types of restenosis which are associated with the IL-1RN (VNTR) allele 1.

The specification also does not teach the existence of the IL-1RN (VNTR) allele 1 in non-human subjects and does not provide any guidance as to how to use the IL-1RN (VNTR) allele 1 to diagnose restenosis in non-human subjects.

Regarding alleles in linkage disequilibrium with the IL-1RN (VNTR) allele 1, the specification teaches only that the IL-1RN (+2018) allele 1 is in 100% linkage disequilibrium with the IL-1RN (VNTR) allele 1. In view of the unpredictability in the art in extrapolating the findings regarding IL-1 alleles to other IL-1 and non-IL-1 alleles, there is insufficient guidance provided in the specification as to additional alleles could be used to specifically infer the presence of the IL-1RN (VNTR) allele 1 and which could thereby be used to diagnose restenosis.

To identify additional polymorphisms which are diagnostic for restenosis and which are in linkage disequilibrium with the IL-1RN (VNTR) allele 1 would require extensive experimentation. For example, such experimentation may involve analyze any of the possible inflammatory diseases in order to identify a disease in which there is an increase in production of any of the possible interleukins, sequencing any of the possible interleukin genes or associated genes, including Il-1A, IL-1B, IL-1RN, Il-6, and IL-10 in patients having the identified inflammatory disease, sequencing the interleukin gene or genes or other genes in normal, control individuals, comparing the sequences of these two groups, and then identifying variations which are present only in the affected group and not in the control group. While methods for identifying polymorphisms are known in the art, such methods provide only the general guidelines that allow researchers to randomly search for polymorphisms that may linked to a disease or to another polymorphism. The results of performing such methodology is highly unpredictable. The specification has provided only an invitation to experiment. The specification does not provide a predictable means for identifying additional

polymorphisms or haplotypes and using these polymorphisms or haplotypes to screen for susceptibility to restenosis.

Working Examples:

Again, the specification teaches kits for determining an increased risk of restenosis in human subjects having SVD wherein the kits comprise an oligonucleotide consisting of SEQ ID NO: 7 or 8, and wherein said oligonucleotide hybridizes 5' or 3' to the IL-1RN (VNTR) allele 1. However, the specification does not provide any working examples in which the IL-1RN (VNTR) allele is detected as indicative of restenosis in any subjects that do not have SVD (e.g., subjects having MVD) or in any non-human subjects. Additionally, the specification does not provide any working examples in which alleles in linkage disequilibrium with the IL-1RN (VNTR) allele 1 are detected and are found to be diagnostic for restenosis.

Conclusions:

Case law has established that '(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that '(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that '(I)t is the specification, not the knowledge of

one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

In the instant case, the specification has identified only one allele, IL-1RN (VNTR) allele 1, which may be useful for diagnosing susceptibility to restenosis in SVD patients. Thereby, the scope of the claims does not bear a reasonable correlation to the scope of enablement provided by the specification and undue experimentation would be required to practice the full scope of the claims because this would require randomized searching of IL-1 genes and the entire genome for additional alleles which may show an association with restenosis. Again, the specification illustrates the unpredictability in establishing a correlation between an IL-1 alleles and the occurrence of cardiovascular disease in that the specification teaches that while one allele has been found to be correlated with restenosis, other alleles characterized as being in linkage disequilibrium with said allele are not correlated with restenosis. In addition, the specification clearly teaches that while one allele may be correlated with a particular type of cardiovascular disease, that same allele may not be correlated with a different type of cardiovascular disease. The specification has not provided any specific data clearly establishing a correlation between alleles in linkage disequilibrium with the IL-1RN (VNTR) allele (e.g., IL-1B (-511), IL-1B (+3954), IL-1B (+4845) alleles) and the occurrence of restenosis and no working examples are provided in the specification in which alleles other than the IL-1RN (VNTR) allele 1 have been successfully employed to determine the presence or predisposition to restenosis. Accordingly, in view of the lack of information in the specification as to how to reasonably identify other alleles correlated with restenosis

without undue experimentation and in view of the unpredictability in the art in correlating the presence of an allele with a disease, particularly in correlating the presence of an IL-1 polymorphism with restenosis, the specification has not adequately taught one of skill in the art how to practice the claimed invention as it is broadly claimed.

Claim Interpretation

8. It is noted that the recitation in the claims of "for determining the existence of or a susceptibility to developing a restenosis" merely sets forth the intended use or purpose of the claimed kits, but does not limit the scope of the claims. As stated in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999), if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation." Accordingly, this recitation has not been given weight with respect to the novelty or obviousness of the claimed kits.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8-10 and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by the GIBCO BRL Catalog (1995/1996; pages 18-15 to 18-16).

The GIBCO BRL Catalog discloses a kit for labeling DNA wherein the kit comprises: a) a random primer solution (i.e., primers which hybridize 3' and 5' to the IL-1A (+4845) alleles and alleles in linkage disequilibrium with the IL-1A (+4845) allele 2): b) biotin-14-dCTP (i.e., a detection means for performing a sequencing or primer extension specific method or an amplification means); c) dNTPs and DNA polymerase (i.e., a detection means for performing a sequencing or primer extension specific method or an amplification means); and d) a control DNA. It is a property of the primers present in the random primer solution that the primers hybridize to sequences in a range of about 50 to 1000 base pairs. Accordingly, the GIBCO BRL kit anticipates the claimed invention.

10. Claims 8-15 are rejected under 35 U.S.C. 102(b) as being anticipated by the Cominelli et al (WO 97/25445).

Cominelli (pages 12-13) discloses a kit for detecting an IL-1RN (VNTR) allele 1 (referred to therein as "IL-IRa") wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Cominelli teaches that the primers consist of SEQ ID NO: 1 and 2 therein (see page 17). It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs (see pages 8 and 10).

Regarding claim 11, the primer of SEQ ID NO: 1 of Cominelli is identical to presently claimed SEQ ID NO: 7 (see page 17).

11. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Duff et al (PGPUB 20050064453).

Duff (paragraph [0016], [0115] and [0116])discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Duff teaches that the primers consist of SEQ ID NO: 9 and 10 therein (see paragraph [0116]). It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs.

Regarding claim 11, the primer of SEQ ID NO: 9 of Duff is identical to presently claimed SEQ ID NO: 7 (see paragraph 93).

Additionally, regarding the recitation in the claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, Duff (paragraph [0115]) teaches kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of Duff which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the claimed invention.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

12. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Duff et al (U.S. Patent No. 6730476).

Duff (paragraphs 17, 92 and 93) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Duff teaches that the primers consist of SEQ ID NO: 9 and 10 therein (see paragraph 93). It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs.

Regarding claim 11, the primer of SEQ ID NO: 9 of Duff is identical to presently claimed SEQ ID NO: 7 (see paragraph 93).

Additionally, regarding the recitation in the claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, Duff (paragraph 92) teaches kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of Duff which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the claimed invention.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

13. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Duff et al (U.S. Patent No. 6268142).

Duff (paragraphs 16-17 and 83) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Duff teaches that the primers consist of present SEQ ID NO: 7 and 8 (referred to therein as SEQ ID NO: 22 and 23) . It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs (see paragraph 83).

Regarding claim 11, the primer of SEQ ID NO: 22 of Duff is identical to presently claimed SEQ ID NO: 7 (see paragraph 144).

Additionally, regarding the recitation in the claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, Duff (see, e.g., paragraphs 17-18) teaches kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele,

which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of Duff which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the claimed invention.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

14. Claims 8-15 are rejected under 35 U.S.C. 102(b) as being anticipated by anticipated by Duff et al (U.S. Patent No. 5698399).

Duff (paragraph 17, 7 and 8) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a control.

Regarding claim 10, Duff teaches that the primers consist of present SEQ ID NO: 7 and 8 (referred to therein as SEQ ID NO: 1 and 2; see paragraphs 42 and 43) . It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs (see paragraph 83).

Regarding claim 11, the primer of SEQ ID NO: 1 of Duff is identical to presently claimed SEQ ID NO: 7 (see paragraph 42).

15. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Duff et al (U.S. Patent No. 6713253).

Duff (see abstract and paragraphs 15 and 41) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Duff teaches that the primers consist of present SEQ ID NO: 7 and 8 (referred to therein as SEQ ID NO: 5 and 6) . It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs (see paragraph 83).

Regarding claim 11, the primer of SEQ ID NO: 5 of Duff is identical to presently claimed SEQ ID NO: 7.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

16. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Duff et al (U.S. Patent No. 6210877).

Duff (see abstract and paragraphs 29 and 15) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Duff teaches that the primers consist of present SEQ ID NO: 7 and 8 (referred to therein as SEQ ID NO: 1 and 2) . It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs (see paragraph 83).

Regarding claim 11, the primer of SEQ ID NO: 1 of Duff is identical to presently claimed SEQ ID NO: 7.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

17. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Francis (PG PUB No. 20060252055).

Francis (see, e.g., paragraph [0037]) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a

hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Francis teaches that the primers consist of present SEQ ID NO: 7 and 8 (referred to therein as SEQ ID NO: 1 and 2) . It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs (see paragraph 83).

Regarding claim 11, the primer of SEQ ID NO: 1 of Francis is identical to presently claimed SEQ ID NO: 7.

Additionally, regarding the recitation in the claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, Francis (see, e.g., paragraphs [0120] and [0142]) teaches kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of Duff which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the claimed invention.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

18. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Duff et al (U.S. Patent No. 6706478).

Duff (paragraphs 16-17 and 83) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Duff teaches that the primers consist of present SEQ ID NO: 7 and 8 (referred to therein as SEQ ID NO: 22 and 23) . It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs (see paragraph 83).

Regarding claim 11, the primer of SEQ ID NO: 22 of Duff is identical to presently claimed SEQ ID NO: 7 (see paragraph 144).

Additionally, regarding the recitation in the claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, Duff (see, e.g., paragraphs 17-18) teaches kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of Duff which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the claimed invention.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in

the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

19. Claims 8-15 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by Duff et al (PGPUB NO. 20040152124).

Duff (paragraphs [0013] and [0015]) discloses a kit for detecting an IL-1RN (VNTR) allele 1 wherein the kit comprises: a) primers that hybridize 5' or 3' of the IL-1RN (VNTR) allele; b) probes and labels (i.e., a detection means for performing a hybridization method); c) reagents for performing an amplification reaction; and d) a positive and/or negative control.

Regarding claim 10, Duff teaches that the primers consist of present SEQ ID NO: 7 and 8 (referred to therein as SEQ ID NO: 22 and 23) . It is a property of these primers that they hybridize to sequences in a range of about 50 to 1000 base pairs.

Regarding claim 11, the primer of SEQ ID NO: 22 of Duff is identical to presently claimed SEQ ID NO: 7 (see paragraph [0158]).

Additionally, regarding the recitation in the claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, Duff (see, e.g., paragraphs 17-18) teaches kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of Duff which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the claimed invention.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Double Patenting

20. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.32 (c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 8-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of U.S. Patent No. 6,268,142.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '142 are both inclusive of kits comprising primers that hybridize 5' and 3' to the IL-1RN (VNTR) allele. In particular, the present claims and the claims of '142 are both inclusive of the primer of present SEQ ID NO: 7 (referred to in '142 as "SEQ ID NO: 22). The claims of '142 do not specifically recite that the kit further includes detection means, amplification means or a control. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have included detection means, amplification means and controls in the kits of '142 in order to have facilitated using the kits for the detection of the IL-1RN (VNTR) allele.

Additionally, regarding the recitation in the present claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, the claims of '142 further encompass kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of '142 which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the present claims.

21. Claims 8-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-13 of U.S. Patent No. 6,746,839. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the claims of '839 are both inclusive of kits comprising primers that hybridize 5' and 3' to the IL-1RN (VNTR) allele. In particular, the present claims and the claims of '839 are both inclusive of the primer of present SEQ ID

NO: 7 (referred to in '839 as "SEQ ID NO: 13). Further, the kits of '839 include a detection means, an amplification means and a control. Additionally, regarding the recitation in the present claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, the claims of '839 encompass kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of '839 which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the present claims.

22. Claims 8-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of copending U.S. Application No. 10/838,503. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of '503 are both inclusive of kits comprising a primer that hybridizes 5' and/or 3' of the IL-1RN (VNTR) allele 1, a detection means, an amplification means and a control. In particular, both the present claims and the claims of '503 encompass kits which comprise the primer of present SEQ ID NO: 7 (referred to in '503 as SEQ ID NO: 5).

Additionally, regarding the recitation in the present claims of an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1, the claims of '503 further encompass kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Thereby, the additional kits of '503 which comprise primers that that hybridize 5' and 3' to the IL-1RN (+2018) allele also anticipate the present claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

23. Claims 8-10 and 12-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 15-20 of copending U.S. Application No. 10/914,396. Although the conflicting claims are not identical, they are not patentably distinct from each other. The present claims are inclusive of kits comprising primers which hybridize 5' or 3' to an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. The claims of '396 encompass kits containing primers that hybridize 5' and 3' to the IL-1RN (+2018) allele, which is an allele in linkage disequilibrium with an IL-1RN (VNTR) allele 1. Further, the present claims and the claims of '396 encompass kits that additionally comprise a detection means, an amplification means and a control.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1634

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